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Applicant: Köster *et al.*

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For: A COMBINATORIAL PROTECTING GROUP STRATEGY FOR MULTIFUNCTIONAL MOLECULES

Art Unit: 1627

Examiner: Ponnaluri, P.

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08/27/01
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Rita Jennings

MARKED UP PARAGRAPHS AND CLAIMS IN ACCORDANCE WITH 37 C.F.R. §1.121

Please amend the paragraph at page 28, line 16 through page 29, line 23 as follows:

^{1}H (400 and 250 MHz) and ^{13}C)101 and 63 MHz) NMR spectra were recorded on a Bruker AMX 400 and a AC 250-P instrument. Samples were dissolved in the presence of tetramethylsilane as internal standard, unless otherwise stated. ^{31}P NMR spectra were recorded on a Varian Gemini 200 instrument. Internal standard: phosphoric acid in the solvent used for the sample (δ = 0.00 ppm), Chemical shifts are given in ppm. Mass spectra were obtained on a Finnigan MAT 311A mass spectrometer under EI conditions, a VG Analytical 70-250S mass spectrometer under FAB conditions (matrix: 3-nitro-benzyl alcohol, Xenon bombardment) and a Finnigan MAT Vision 2000 mass spectrometer under MALDI-TOF conditions (matrix solution: 0.7 mol/ 13-hydroxy picolinic acid and 0.07 mol/ 1 ammonium citrate in acetonitrile/ water, 1/1, v/v). Elementary analyses were performed by the analytical department of the Institute of Organic Chemistry, University of Hamburg. Thin layer chromatography (tlc) was carried out on 60 PF_{254} silica gel coated alumina sheets (Merck, Darmstadt, No 5562). Trityl and sugar containing compounds are visualized with sugar spray reagent (0.5 ml 4-metoxybenzaldehyde, 9 ml

ethanol, 0.5 ml concentrated sulfuric acid and 0.1 ml glacial acetic acid) by heating with a fan or on a hot plate. p-Nitrophenyl ester containing compounds are visualized by ammonia vapour. Column chromatography was performed using silica gel from Merck. HPLC results were obtained on a Waters chromatography systems 625 LC with a photodiodearray detector 996 and using reversed phase columns ([Waters Nova-Pak C18] WATERS NOVA-PAK C18® (octadecyl silica gel) column, 60 Å, 4 μm particles, 3.9 x 300mm, software: [Millenium] MILLENIUM® 2.0, eluants were: 0.1 M triethylammonium acetate at pH 7.0 (A) and acetonitrile (B); the column was equilibrated at 30°C at 1ml per min, with 95% A/ 5% B, v/v, with elution using a linear gradient from 5% to 40% B in 40 min, monitored at 254 nm). Spectrophotometric measurements in the UV/ Vis region were performed on a Beckman UV35 and a LKB Ultrospec Plus UV/ Vis spectrophotometer. Solvents were dried and purified before use according to standard procedures. Extractions were monitored by tlc to optimize completion of extraction.

Please amend claims 4, 11-16 and 26-28 as follows:

4. (Amended) A process [of claim 3, wherein the low molecular weight compound is] for generating a combinatorial library, comprising the steps of:

(a) preparing a plurality of immobilized molecules selected from [the group consisting of a saccharide, aminosugar, deoxysugar,] a nucleoside[,] and a nucleotide[, coenzyme, amino acid, lipid, steroid, vitamin, hormone, alkaloid and small molecule drug compound]; wherein each molecule contains 3 to 10 reactive moieties, each reactive moiety being blocked by a blocking group, wherein at least three of the blocking groups on each immobilized molecule are independently removable under at least three different conditions; and

(b) removing each blocking group and derivatizing the resulting reactive moiety in a preprogrammed, regioselective manner; wherein each member of the plurality of immobilized molecules is uniquely derivatized at at least one reactive moiety with a unique substituent, thereby generating a combinatorial library.

11. (Amended) A process of claim [1 or 2] 4, wherein the reactive moieties are selected from [the group consisting of] OH, SH, NH_2, CO_2H, SOH, SO_2H, SO_3H, CHO, keto, phosphate, phosphite, phosphoamidite, halogen, CN, CNS, NCS[,] and NCO [and derivatives thereof].

12. (Amended) A process of claim [1 or 2] 4, wherein the [molecule has] immobilized molecules have been immobilized based on linkage to a solid support.

13. (Amended) A process of claim 12, wherein the solid support is selected from beads, flat supports, [wafers with or without pits and/or channels, the bottom of a microtiter plate or] wafers with pits, wafers without pits, wafers with channels, wafers without channels, bottom surface of a microtiter plate, and [the] inner walls of a capillary.

14. (Amended) A process of claim 13, wherein the beads are comprised of a material selected from polystyrene, polyamide, cellulose, [Sephadex, Sepharose] agarose, dextran cross-linked with epichlorohydrin, silica gel, controlled pore glass (CPG), and [teflon] polytetrafluoroethylene.

15. (Amended) A process of claim 12, wherein the linkage [can be cleaved] is cleavable under acidic, alkaline, neutral or photolytic conditions.

16. (Amended) A process of claim 15, wherein the linkage is selected from [the group consisting of] trityl ether, ester, β-benzoylpropionyl, levulinyl, disulfide[,] and sulfenyl [and derivatives thereof].

26. (Amended) A combinatorial [set of compounds according to claim 23] library wherein the compounds comprising the library are selected from [the group consisting of a: saccharide, aminosugar, deoxysugar, nucleoside,

nucleotide, coenzyme, amino acid, lipid, steroid, vitamin, hormone, alkaloid and small molecule drug compound] nucleosides and nucleotides, wherein each compound has from 3 to 10 reactive moieties having blocking groups on the reactive moieties, wherein at least three blocking groups are independently removable under different conditions, thereby allowing selective derivatization after deblocking, and wherein one reactive moiety is utilized for immobilization.

27. (Amended) A combinatorial [set of oligomeric compounds] library according to claim [23] 26, [selected from the group consisting of an oligosaccharide, oligopeptide and oligonucleotide] wherein the compounds of the library are oligonucleotides.

28. (Amended) A combinatorial [set of oligomeric compounds] library of claim [23] 26 in which at one or more positions in the sequence a preselected set of building blocks is incorporated.